REMARKS

In an Office Action dated September 25, 2009, the Examiner correctly stated the status of the claims; Claims 1 and 3-21 are pending, Claim 2 is cancelled, Claims 5, 6, 11, and 14-16 are withdrawn, and Claims 1, 3-4, 7-10, 12-13, and 17-21 are under consideration. The Examiner withdrew all rejections of record in view of Applicants' response, but imposed new objections and rejections allegedly necessitated by Applicants' amendments. Although Claim 21 is designated as "rejected" in the disposition of claims statement, it is not included among any of the Examiner's rejections. In light of the amendments above and for the reasons noted below, Applicants respectfully request reconsideration.

Objections

Claims 1, 3, 4, 8, and 12 are objected to because according to the Examiner, the marker gene must be located between the 5' and 3' flanking arms. The amended claims reflect the presence of the marker on the insert between the flanking arms.

The Examiner objected to Claims 1, 7, and 17 because the pending claims recite that clumps of cells are being electroporated but not that the construct integrates into multiple genomes. The proposed recitation is not adopted and should not be required. The Examiner's reading of the claims is inaccurate. While multiple copies of the genetic construct can be electroporated into clumps of cells, once inside a single cell, the electroporated copy or copies of the construct can homologously recombine with only the one stem cell genome of that cell.

Claim 3 is objected to for alleged lack of clarity. Claim 3 is amended, substantially as suggested by the Examiner. The Examiner objected to Claims 4 and 8 for alleged grammatical inaccuracies. Applicants amend Claims 4 and 8 as indicated above to address the Examiner's objections.

The Examiner further objected to Claim 8 as "confusing the purpose of Claim 12" (Office Action, page 3 third paragraph). Applicants respectfully maintain for the following reasons that Claim 8, which depends from independent Claim 7, does not confuse the purpose of Claim 12. Claim 7 and its dependents recite methods for purifying defined lineage cells using an expressed marker gene; Claim 8 simply specifies one structure that facilitates expression of the marker

gene in the cells to be purified in a Claim 7 method. Defined lineage cells purified in such a method can express not only the marker gene employed in the purification, but many other genes characteristic of the lineage. A skilled person can identify other genes characteristically expressed in the cells of the defined lineage.

Claim 12 relates to methods for purifying cells on the basis of such characteristic expression from a population of cells that includes some cells of the defined lineage (identified by expression of the lineage-specific genes). The "culture that comprises differentiated cells" in step (b) of Claim 12 does not consist exclusively of terminally differentiated cells, but rather comprises cells of various stages, that could include differentiated cells, partially differentiated cells and cells that remain undifferentiated, or have not yet differentiated, in response to the differentiating conditions. Cells that have undergone only partial lineage commitment can be considered relatively undifferentiated. Since the cells purified in the methods of Claim 12 can be of any defined lineage, it follows that those cells can also be undifferentiated cells, as is contemplated in the specification which discloses an example in which ES cells were cultured under differentiating conditions and undifferentiated cells were isolated (paragraphs [0037]-[0040]).

Claim 13 is objected to for allegedly failing to further limit Claim 12 from which it depends. Specifically, the Examiner alleged that the species of cells recited in Claim 13 (i.e., undifferentiated cells) are not encompassed by the species recited in Claim 12. Applicants respectfully disagree for the reasons explained above. The genes specified in Claim 13 are some genes that can a skilled person can identify as characteristically expressed in defined lineage cells.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected Claims 1, 4, 7, 8, 10, 12, and 17-20 for alleged obviousness over Smith *et al.*, in view of either Jaynes *et al.* or Chalitta-Eid, as evidenced by Tenner *et al.* or Tajima *et al.* further in view of Prasad *et al.* and Takada *et al.* Claims 3, 9, and 13 are rejected for alleged obviousness over Smith *et al.*, in view of either Jaynes *et al.* or Chalitta-Eid (as evidenced by Tenner *et al.*) and further in view of West *et al.*

In a previous response, Applicants amended the claims to recite specifics of the electroporation methods not taught or suggested by Smith, Jaynes, Chalitta-Eid, and Tenner.

The claims specify that the cells are electroporated in clumps. Certain claims recite electroporation settings. Upon consideration of these recitations, the Examiner withdrew all rejections of record but alleged that it would be obvious to electroporate clumps of hES cells because it was known to grow hES cells in clumps, as allegedly evidenced by Thomson, and to electroporate adult rat parotid gland cells in clumps, allegedly taught by Prasad. The Examiner relied on Tajima as allegedly teaching the use of a single pulse at 320 V and 250 μF.

Neither Thomson nor Prasad teach or suggest electroporating clumps of hES cells. Thomson teaches growing hES cells in colonies, not clumps. Footnote 6 (not reference 16) explains that "inner cell mass-derived outgrowths were dissociated into clumps," which were subsequently replated onto murine fibroblasts to form colonies. Thomson does not teach or suggest culturing, much less electroporating, hES cells in clumps. Prasad does not teach, as alleged (Office Action, page 5, third paragraph), that electroporation requires use of cell clumps. In fact, Prasad teaches that rat parotid cells can be electroporated as clumps or as single-cell suspension (Prasad, page 321, right column). Importantly, Prasad does not teach or suggest electroporating hES cells. At the time of filing, a skilled artisan would not have had a reasonable expectation of success in using rat adult cell protocols to electroporate human embryonic stem cells, especially since murine ES cell protocols were known to not work for human ES cells.

Tajima does not, as alleged, teach a range "that touches or overlaps the claimed range" (Office Action, page 6, last paragraph; presumably relying on MPEP § 2131.03). In fact, Tajima does not teach any range, but rather a single microfarad value distinct from that recited in the claims. Claims 19-21 recite using a single 320 V and 200 μF pulse, not 250 μF. The Examiner failed to explain how using 250 μF renders obvious using 200 μF.

By withdrawing all previous rejections, the Examiner acknowledged that the claims are not obvious in view of Smith, Jaynes, Chalitta-Eid, Tenner, and West alone. Reconsideration is respectfully requested.

Fees

A Petition for an extension of time for one month accompanies this response so the response will be deemed to have been timely filed. If any other extension is due in this or any

subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee due to Deposit Account No. 17-0055. No other fee is believed due, but if any other fee is due in this or any subsequent response, please consider this to be a request to charge the fee to the same Deposit Account.

Respectfully submitted,

/Bennett J. Berson/

Bennett J. Berson
Reg. No.: 37,094
Attorney for Applicants
QUARLES & BRADY LLP
P.O. Box 2113
Madison, WI 53701

TEL 608/251-5000
FAX 608/251-9166